We claim:

1. An isolated human monoclonal antibody which binds to human CD25 and inhibits IL-2 binding to CD25.

2. The antibody of claim 1, selected from the group consisting of an IgG1, an IgG2, an IgG3, an IgG4, an IgM, an IgA1, an IgA2, a secretory IgA, an IgD, and an IgE antibody.

3. The antibody of claim 2, wherein the antibody is an IgG1 antibody.

4. The antibody of claim 2, wherein the antibody is an IgG4 antibody.

5. The antibody of claim 1, wherein the antibody dissociates from human CD25 with a dissociation equilibrium constant (K_D) of about 10^{-8} M or less, preferably of about 10^{-9} M or less, and more preferably of about 10^{-10} M or less, or 10^{-11} M or even less, when determined by surface plasmon resonance (SPR) technology in a BIAcore 3000 instrument using human recombinant CD25 as the ligand and the antibody as the analyte.

6. The antibody of claim 1, wherein the antibody has one or more of the following characteristics:

(a) specificity for human CD25;

(b) inhibits binding of IL-2 to CD25;

(c) eliminates T cells expressing CD25;

(d) tolerizes T cells;

(e) inhibits proliferation of T cells expressing CD25;

(f) inhibits anti-CD3 antibody-induced T cell proliferation of peripheral blood mononuclear cells (PBMCs);

(g) inhibits mixed lymphocyte reaction (MLR);

(h) internalization of CD25 expressed on T cells.

7. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:5 and SEQ ID NO:7, respectively, or conservative sequence modifications thereof.

8. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:13 and SEQ ID NO:15, respectively, or conservative sequence modifications thereof.

9. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:1 and SEQ ID NO:3, respectively, or conservative sequence modifications thereof.

10. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:9 and SEQ ID NO:11, respectively, or conservative sequence modifications thereof.

11. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:6 and SEQ ID NO:8, respectively, or conservative sequence modifications thereof.

12. The antibody of claim 11 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous, preferably at least 95% homologous, and more preferably at least 98%, or at least 99% homologous to the amino acid sequences as set forth in SEQ ID NO:6 and SEQ ID NO:8, respectively.

13. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:14 and SEQ ID NO:16, respectively, or conservative sequence modifications thereof.

14. The antibody of claim 13 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous, preferably at least 95% homologous, and more preferably at least 98%, or at least 99% homologous to the amino acid sequences as set forth in SEQ ID NO:14 and SEQ ID NO:16, respectively.

15. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:2 and SEQ ID NO:4, respectively, or conservative sequence modifications thereof.

16. The antibody of claim 15 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous, preferably at least 95% homologous, and more preferably at least 98%, or at least 99% homologous to the amino acid sequences as set forth in SEQ ID NO:2 and SEQ ID NO:4, respectively.

17. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:10 and SEQ ID NO:12, respectively, or conservative sequence modifications thereof.

18. The antibody of claim 17 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous, preferably at least 95% homologous, and more preferably at least 98%, or at least 99% homologous to the amino acid sequences as set forth in SEQ ID NO:10 and SEQ ID NO:12, respectively.

19. The antibody of claim 1 comprising at least one human variable region selected from the group consisting of:

(i) SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, and 16; and

(ii) a sequence which is at least 90% homologous, preferably at least 95% homologous, and more preferably at least 98%, or at least 99% homologous to any one of the amino acid sequences as set forth in (i).

20. An isolated human monoclonal antibody which binds to an epitope on human CD25 defined by the antibody of claim 7.

21. An isolated human monoclonal antibody which has the binding characteristics of the antibody of claim 7.

22. An isolated human monoclonal antibody which binds to human CD25 comprising at least one CDR sequence selected from the group consisting of:

(i) SEQ ID NOs: 23, 24, 25, 26, 27, or 28; or

(ii) conservative sequence modifications of any one of the sequences defined in (i).

23. The antibody of claim 22, comprising a V_H CDR3 of SEQ ID NO: 25, a conservative sequence modification thereof, or a sequence which has 1-3 amino acid substitutions, deletions or additions compared to the V_H CDR3 of SEQ ID NO:25.

24. The antibody of claim 23, comprising a V_H CDR3 having the amino acid sequence

X_1-Asp-Trp-X_2-Asp-X_3

wherein X_1 is Arg, His or Lys; X_2 is Gly, Ala, Val, Leu, Ile, Tyr, Trp or Phe; and X_3 is Pro, Tyr, Phe or Trp.

25. The antibody of claim 24, wherein X_1 is Arg or Lys; X_2 is Gly or Phe; and X_3 is Pro or Tyr.

26. The antibody of claim 22, comprising at least four CDRs selected from (i) V_H CDR1, CDR2, and CDR3 and V_L CDR1, CDR2 and CDR3 of SEQ ID NOs: 23, 24, 25, 26, 27, and 28; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

27. The antibody of claim 22, comprising (i) V_H CDR1, CDR2 and CDR3 and V_L CDR1, CDR2 and CDR3 of SEQ ID NOs: 23, 24, 25, 26, 27, and 28; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

28. An isolated human monoclonal antibody which binds to human CD25 comprising at least one CDR sequence selected from the group consisting of:

(i) SEQ ID NOs: 29, 30, 31, 32, 33, or 34; or

(ii) conservative sequence modifications of any one of the sequences defined in (i).

29. The antibody of claim 28, comprising a V_H CDR3 of SEQ ID NO: 31, a conservative sequence modification thereof, or a sequence which has 1-3 amino acid substitutions, deletions or additions compared to the V_H CDR3 of SEQ ID NO:31.

30. The antibody of claim 28, comprising at least 4 CDR sequences selected from (i) V_H CDR1, CDR2, and CDR3 and V_L CDR1, CDR2, and CDR3 of SEQ ID NOs: 29, 30, 31, 32, 33, and 34; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

31. The antibody of claim 28, comprising (i) V_H CDR1, CDR2 and CDR3 and V_L CDR1, CDR2 and CDR3 of SEQ ID NOs: 29, 30, 31, 32, 33, and 34; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

32. An isolated human monoclonal antibody which binds to human CD25 comprising at least one CDR sequence selected from the group consisting of:

(i) SEQ ID NOs: 35, 36, 37, 38, 39, or 40; or

(ii) conservative sequence modifications of any one of the sequences defined in (i).

33. The antibody of claim 32, comprising a V_H CDR3 of SEQ ID NO: 37, a conservative sequence modification thereof, or a sequence which has 1-3 amino acid substitutions, deletions or additions compared to the V_H CDR3 of SEQ ID NO:37.

34. The antibody of claim 32, comprising at least 4 CDR sequences selected from (i) V_H CDR1, CDR2, and CDR3 and V_L CDR1, CDR2, and CDR3 of SEQ ID Nos: 35, 36, 37, 38, 39, and 40; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

35. The antibody of claim 32, comprising (i) V_H CDR1, CDR2 and CDR3 and V_L CDR1, CDR2 and CDR3 of SEQ ID NOs: 35, 36, 37, 38, 39, and 40; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

36. An isolated human monoclonal antibody which binds to human CD25 comprising at least one CDR sequence selected from the group consisting of:

(i) SEQ ID NOs: 17, 18, 19, 20, 21, or 22; or

(ii) conservative sequence modifications of any one of the sequences defined in (i).

37. The antibody of claim 36, comprising a V_H CDR3 of SEQ ID NO: 19, a conservative sequence modification thereof, or a sequence which has 1-3 amino acid substitutions, deletions or additions compared to the V_H CDR3 of SEQ ID NO:19.

38. The antibody of claim 36, comprising at least four CDR sequences selected from (i) SEQ ID NOs: 17, 18, 19, 20, 21, and 22; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

39. The antibody of claim 36, comprising (i) V_H CDR1, CDR2 and CDR3 and V_L CDR1, CDR2 and CDR3 of SEQ ID NOs: 17, 18, 19, 20, 21, and 22; or (ii) conservative sequence modifications of any one of the sequences defined in (i).

40. The antibody of claim 1 comprising a V_H CDR1 domain having the amino acid sequence

X_1-Tyr-X_2-Ile-X_3

wherein X_1, X_2 and X_3 are natural amino acids; and

wherein X_1 is different from Ser; or X_2 is different from Ala; or X_3 is different from Ser.

41. The antibody of claim 40, wherein X_1 is Arg, Lys or His; X_2 is Ala, Gly, Val, Leu, Ile, or Pro; and X_3 is Asn or Gln.

42. The antibody of claim 41, wherein X_1 is Arg; X_2 is Ala, Ile, or Pro; and X_3 is Asn.

43. The antibody of claim 1 comprising a V_H CDR2 domain having the amino acid sequence

Arg-Ile-Ile-Pro-Ile-Leu-Gly-X_1-X_2-X_3-Tyr-Ala-Gln-X_4-Phe-Gln-X_5

wherein X_1, X_2, X_3, X_4, and X_5 are natural amino acids; and

wherein X_1 is different from Ile; or X_2 is different from Ala; or X_3 is different from Asn; or X_4 is different from Lys; or X_5 is different from Gly.

44. The antibody of claim 43, wherein X_1 is Ile, Val, Gly, Ala or Leu; X_2 is Ala, Ile, Val, Gly, Leu, Glu or Asp; X_3 is Asp, Glu, Asn or Gln; X_4 is Lys, Arg or His; and X_5 is Gly, Ile, Val, Ala, Leu, Asp or Glu.

45. The antibody of claim 44, wherein X_1 is Ile or Val; X_2 is Ala or Glu; X_3 is Asp or Asn; X_4 is Lys or Arg; and X_5 is Gly or Asp.

46. The antibody of claim 1 comprising a V_L CDR1 domain having the amino acid sequence

Arg-Ala-Ser-Gln-Ser-X_1-Ser-Ser-X_2-Leu-Ala

wherein X_1 and X_2 are natural amino acids; and

wherein X_1 is different from Val; or X_2 is different from Tyr.

47. The antibody of claim 46, wherein X_1 is Val, Ala, Leu, Ile or Gly; and X_2 is Phe, Trp or Tyr.

48. The antibody of claim 47, wherein X_1 is Val or Gly; and X_2 is Phe or Tyr.

49. The antibody of claim 1 comprising a V_L CDR3 domain having the amino acid sequence

Gln-Gln-Tyr-X_1-Ser-Ser-Pro-X_2-X_3

wherein X_1 is Gly, Ala, Val, Leu, Ile, Ser or Thr; X_2 is Leu, Gly, Ala, Val or Ile; and X_3 is Thr or Ser.

50. The antibody of claim 49, wherein $X_1$is Gly or Ser, X_2 is Leu or Ile; and X_3 is Thr.

51. An isolated human antibody comprising a heavy chain variable region amino acid sequence derived from a human V_H1-69/JH4b or V_H1-69/JH5b germline sequence and a light chain variable region amino acid sequence derived from a human A27/J_K4 or A27/J_K5 germline sequence, wherein the human antibody binds to human CD25.

52. An isolated human antibody comprising a heavy chain variable region amino acid sequence derived from a human V_H1-69/D7-27/JH4b or V_H1-69/ D7-27/JH5b germline sequence and a light chain variable region amino acid sequence derived from a human A27/J_K4 or A27/J_K5 germline sequence, wherein the human antibody binds to human CD25.

53. The antibody of claim 1 which is an intact antibody selected from the group consisting of an intact IgG1 antibody, an intact IgG2 antibody, an intact IgG3 antibody, an intact IgG4 antibody, an intact IgM antibody, an intact IgA1 antibody, an intact IgA2 antibody, an intact secretory IgA antibody, an intact IgD antibody, and an intact IgE antibody, wherein the antibody is glycosylated in a eukaryotic cell.

54. The antibody of claim 1 which is an intact antibody selected from the group consisting of an intact IgG1,κ antibody, an intact IgG1,λ antibody, an intact IgG4,κ antibody, and an intact IgG4,λ antibody, wherein the antibody is glycosylated in a eukaryotic cell.

55. The antibody of claim 1 which is an antibody fragment or a single chain antibody.

56. An isolated human monoclonal antibody which binds to human CD25 and inhibits IL-2 binding to CD25 which is a binding-domain immunoglobulin fusion protein comprising (i) a heavy chain variable region or a light chain variable region as defined in claim 19, that is fused to an immunoglobulin hinge region polypeptide, (ii) an immunoglobulin heavy chain CH2 constant region fused to the hinge region, and (iii) an immunoglobulin heavy chain CH3 constant region fused to the CH2 constant region.

57. The antibody of claim 1 produced by a hybridoma which includes a B cell obtained from a transgenic nonhuman animal, in which V-(D)-J gene segment rearrangements have resulted in the formation of a functional human heavy chain transgene and a functional human light chain transgene, fused to an immortalized cell.

58. A hybridoma comprising a B cell obtained from a transgenic nonhuman animal in which V-(D)-J gene segment rearrangements have resulted in the formation of a functional human heavy chain transgene and a functional light chain transgene fused to an immortalized cell, wherein the hybridoma produces a detectable amount of the monoclonal antibody of any one of the preceding claims.

59. A hybridoma which produces a human monoclonal antibody according to claim 1.

60. The antibody of claim 1 produced by a transfectoma comprising nucleic acids encoding a human heavy chain and a human light chain.

61. A transfectoma comprising nucleic acids encoding a human heavy chain and a human light chain, wherein the transfectoma produces a detectable amount of the antibody of claim 1.

62. A eukaryotic or prokaryotic host cell comprising nucleic acids encoding a human heavy chain and a human light chain, wherein the host cell produces a detectable amount of the antibody of claim 1.

63. A transgenic nonhuman animal or plant comprising nucleic acids encoding a human heavy chain and a human light chain, wherein the animal or plant produces a detectable amount of the antibody of claim 1.

64. A method of producing a human monoclonal antibody which binds to human CD25, comprising:

immunizing a transgenic nonhuman animal having a genome comprising a human heavy chain transgene and a human light chain transgene with human CD25 or a cell expressing human CD25, such that antibodies are produced by B cells of the animal;

isolating B cells of the animal;

fusing the B cells with myeloma cells to form immortal, hybridoma cells that secrete human monoclonal antibodies specific for human CD25; and

isolating the human monoclonal antibodies specific for CD25 from the culture supernatant of the hybridoma, or from a transfectoma derived from such hybridoma.

65. A composition comprising the human antibody of claim 1 and a pharmaceutically acceptable carrier.

66. A composition according to claim 65, further comprising a therapeutic agent.

67. The antibody according to claim 1, further comprising a chelator linker for attaching a radioisotope.

68. An immunoconjugate comprising an antibody according to claim 1 linked to a cytotoxic agent, a radioisotope, or a drug.

69. A bispecific or multispecific molecule comprising an antibody according to claim 1 and a binding specificity for CD3, CD4, IL-15R, membrane bound or receptor bound TNF-α, or membrane bound or receptor bound IL-15.

70. A method of inhibiting growth and/or proliferation of a cell expressing CD25, comprising administering an antibody of claim 1, such that the growth and/or proliferation of the cell is inhibited.

71. A method of eliminating a cell expressing CD25, comprising administering an antibody of claim 1, such that killing of the cell expressing CD25 occurs.

72. The method of claim 70, wherein the cell expressing CD25 is an activated T cell.

73. A method of treating or preventing a disorder involving cells expressing CD25, comprising administering an antibody of claim 1, in an amount effective to treat or prevent the disease.

74. The method of claim 73, wherein the disorder is selected from the group consisting of transplant rejection, graft-versus-host disease, an immune, autoimmune or inflammatory disease, an inflammatory or hyperproliferative skin disorder, and a lymphoid neoplasm.

75. The method of claim 74, wherein the transplant rejection is an allograft or xenograft rejection in patients undergoing organ or tissue transplantation, such as heart, lung, combined heart-lung, trachea, kidney, liver, pancreas, oesophagus, bowel, skin, limb, umbilical cord, stem cell, or islet cell transplantation.

76. The method of claim 75 for preventing transplant rejection by prophylactic treatment with the antibody according to any one of the preceding claims.

77. The method of claim 75, wherein the graft-versus-host disease is selected from the group consisting of blood transfusion graft-versus-host disease and bone marrow graft-versus-host disease.

78. The method of claim 74, wherein the immune, autoimmune or inflammatory disease is selected from the group consisting of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, type 1 diabetes, insulin-requiring type 2 diabetes, multiple sclerosis, systemic lupus erythematosus, myasthenia gravis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, dermato-polymyositis, Sjögren's syndrome, arteritides, including giant cell arteritis, aplastic anemia, asthma, scleroderma, and uveitis.

79. The method of claim 74, wherein the inflammatory or hyper-proliferative skin disorder is selected from the group consisting of psoriasis, including plaque psoriasis, pustulosis palmoplantaris (PPP), erosive lichen planus, pemphigus bullosa, epidermolysis bullosa, contact dermatitis, and atopic dermatitis.

80. The method of claim 74, wherein the lymphoid neoplasm is selected from the group consisting of T cell leukemia, Hodgkin's disease, hairy cell leukemia, or cutaneous T cell lymphoma, including mycosis fungoides and Sezary's syndrome..

81. The method of claim 73, wherein the disease is a malignancy wherein an inhibition of infiltrating CD25+ regulatory T cells is beneficial, and which is selected from the group consisting of gastric cancer, esophageal cancers, malignant melanoma, colorectal cancer, pancreas cancer, breast cancer, small cell lung cancer, non-small cell lung cancer, cervical cancer, ovarian cancer, and renal cell carcinoma.

82. The method of claim 73, wherein the disease is a hematological disorder selected from the group consisting of adult T cell leukemia/lymphoma, anaplastic large cell lymphoma, chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), peripheral T cell lymphoma, and secondary amyloidosis.

83. The method of claim 70, further comprising separately administering another therapeutic agent and/or therapy to the subject.

84. The method of claim 83, wherein the therapeutic agent is an immunosuppressant selected from the group consisting of cyclosporine, azathioprine, mycophenolic acid, mycophenolate mofetil, corticosteroids, such as prednisone, methotrexate, gold salts, sulfasalazine, antimalarials, brequinar, leflunomide, mizoribine, 15-deoxyspergualine, 6-mercaptopurine, cyclophosphamide, rapamycin, tacrolimus (FK-506), OKT3, and anti-thymocyte globulin.

85. The method of claim 83, wherein the therapeutic agent is an anti-inflammatory agent selected from the group consisting of a steroidal drug , a NSAID (nonsteroidal anti-inflammatory drug), and a DMARD, such as methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, IL-1 receptor blocking agents, *e.g.*, anakinara, TNF-α blocking agents, *e.g.*, etanercept, infliximab, and adalimumab, anti-IL-6R antibodies, CTLA4Ig, and anti-IL-15 antibodies

86. The method of claim 83, wherein the therapeutic agent is an agent or therapy for treating an inflammatory or hyperproliferative skin disorder selected from the group consisting of coal tar, A vitamin, anthralin, calcipotrien, tarazotene, corticosteroids, methotrexate, retinoids, e.g. acicretin, cyclosporine, etanercept, alefacept, efaluzimab, 6-thioguanine, mycophenolate mofetil, tacrolimus (FK-506), hydroxyurea, and phototherapy, such as UVB (broad-band and narrow-band ultraviolet B), UVA (ultraviolet A) and PUVA (psoralen methoxalen plus ultraviolet A).

87. The method of claim 83, wherein the therapeutic agent is selected from the group consisting of doxorubicin, cisplatin, bleomycin, carmustine, chlorambucil, and cyclophosphamide.

88. A method for detecting the presence of CD25 antigen, or a cell expressing CD25, in a sample comprising:

contacting the sample with the antibody of claim 1 under conditions that allow for formation of a complex between the antibody and CD25; and

detecting the formation of a complex.

89. A diagnostic kit for detecting the presence of CD25 antigen, or a cell expressing CD25, in a sample comprising the antibody of claim 1, wherein the antibody optionally is linked to a detectable label.

90. An expression vector comprising a nucleotide sequence encoding the variable region of a light chain, heavy chain or both light and heavy chains of a human antibody which binds to human CD25.

91. The expression vector of claim 90, further comprising a nucleotide sequence encoding the constant region of a light chain, heavy chain or both light and heavy chains of a human antibody which binds to human CD25.

92. An expression vector comprising a nucleotide sequence encoding a heavy chain variable region comprising a nucleotide selected from the group consisting of the nucleotide sequences as set forth in SEQ ID NOs: 1, 5, 9, or 13, or conservative modifications thereof, and a light variable region comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences as set forth in SEQ ID NOs: 3, 7, 11, or 15, or conservative modifications thereof.

93. An expression vector comprising a nucleotide sequence encoding a heavy chain variable region comprising an amino acid sequence selected from the group consisting of the amino acid sequences as set forth in SEQ ID NOs:2, 6, 10, or 14 and a light chain variable region comprising the amino acid sequence selected from the group consisting of the amino acid sequences as set forth in shown in SEQ ID NOs: 4, 8, 12, or 16, and conservative sequence modifications thereof.

94. An expression vector which encodes a human monoclonal antibody according to claim 1.

95. A pharmaceutical composition comprising the expression vector of claim 90 and a pharmaceutically acceptable carrier.

96. An anti-idiotypic antibody binding to an antibody of claim 1.

97. An anti-idiotypic antibody binding to AB1, AB7, AB11 or AB12.

98. Use of an anti-idiotypic antibody of claim 96 for detecting the level of human monoclonal antibody against CD25 in a sample.